

09/919,505 filed 07/31/2001

Ausserer, et al.

Reply to Office Action of October 28, 2004

Amendment to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (currently amended) A method of separating ~~a one or more sample materials~~ into a plurality of fractions, comprising:
providing a system comprising:
a separation ~~conduit~~ channel having a separation matrix disposed therein
~~and,~~
~~a sample loading conduit~~ an injection channel in fluid communication with the separation ~~conduit~~ channel at an intermediate point along the ~~sample loading conduit~~ injection channel, and
a sample loading channel in fluid communication with the injection channel, a source of a first sample material, and a source of a reagent;
bulk-flowing a transporting the first sample material and the reagent into the sample loading conduit-channel, wherein the first sample material and the reagent form a mixture without substantially displacing the separation matrix from the separation conduit;
injecting a portion of the sample material mixture from the sample loading channel, through the injection channel, into the separation conduit-channel; and
separating the first sample material within the mixture into a plurality of fractions.
2. (currently amended) The method of claim 1, wherein the sample loading ~~conduit-channel~~ comprises a loading end and a waste end, the loading end being contacted with a source of the first sample material, and further comprising applying a first pressure difference across the sample loading ~~conduit-channel~~ to move the first sample material into the loading end of the sample loading channel and toward the waste end of the sample loading channel.
3. (currently amended) The method of claim 1, wherein less than 10% of the separation matrix in the separation ~~conduit-channel~~ is displaced during the

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step of ~~bulk-flowing~~injecting the first sample material into the sample loading ~~conduit~~channel.

4. (currently amended) The method of claim 1, wherein less than 5% of the separation matrix in the separation ~~conduit~~channel is displaced during the step of ~~bulk-flowing~~injecting the first sample material into the sample loading ~~conduit~~channel.

5. (currently amended) The method of claim 1, wherein less than 1% of the separation matrix in the separation conduit is displaced during the step of ~~bulk-flowing~~injecting the first sample material into the sample loading ~~conduit~~channel.

6. (currently amended) The method of claim 1, wherein the separation ~~conduit~~channel is provided with a higher flow resistance than the sample loading ~~conduit~~channel.

7. (currently amended) The method of claim 6, wherein the separation ~~conduit~~channel comprises one or more of a greater length or a smaller cross-sectional area than the sample loading ~~conduit~~channel.

8. (currently amended) The method of claim 1, wherein the sample loading ~~conduit~~channel comprises a loading end and a waste end, the loading end being contacted with a source of the first sample material through a capillary element, and further comprising applying a first pressure difference across the sample loading conduit to move the first sample material through the capillary element into the loading end of the sample loading channel and toward the waste end of the sample loading channel.

9. (currently amended) The method of claim 82, wherein a negative pressure is applied to the waste end of the sample loading ~~conduit~~channel to supply the first pressure difference across the sample loading ~~conduit~~channel.

10. (currently amended) The method of claim 82, wherein the ~~sample loading conduit~~injection channel and the separation ~~conduit~~channel are in fluid communication at a first fluid junction, and further comprising moving a portion of the

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first sample material in the sample-loading conduit-injection channel through the first fluid junction and into the separation conduit.

11. (currently amended) The method of claim 10, wherein the first fluid junction comprises a channel segment connecting the sample-loading conduit with the separation conduitstep of moving a portion of the first sample material through the first fluid junction further comprises applying a pressure differential across the injection channel.

12. (currently amended) The method of claim 10, wherein the step of moving the first sample material from the sample-loading conduit through the fluid junction and into the separation conduitfurther comprises applying a voltage difference through the fluid junction to electrokinetically move the portion of the sample material from the sample-loading conduit into the separation conduitacross the injection channel.

13. (currently amended) The method of claim 12, wherein the step of separating the first sample material comprises applying a voltage difference across the separation conduitchannel, to electrophoretically separate the first sample material into different fractions.

14. (currently amended) The method of claim ~~8~~1, wherein the separation conduit-channel is in fluid communication with a source of separation matrix, and further comprising applying a second pressure difference across the separation conduit-channel to transport an amount of separation matrix into the separation conduit from the source of separation matrix after the first sample material is separated into a plurality of different fractions.

15. (currently amended) The method of claim 1, wherein the sample loading conduit-channel is in fluid communication with at least a first the source of reagent through a reagent channel, and wherein the step of transporting a sample materialintoreagent channel and the sample loading conduit transports an amount of the first reagent into the sample loading conduit to mix with the sample materialchannel have differing flow resistances.

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16. (currently amended) The method of claim ~~15~~1, wherein the ~~first~~ reagent is selected from a standard compound, a diluent, a detergent, or a labeling reagent.

17. (currently amended) The method of claim 1, wherein the sample loading conduit ~~channel~~ has substantially no separation matrix disposed therein.

18. (currently amended) ~~A~~ ~~The method of separating a plurality of samples into different fractions~~ claim 2, further comprising:

~~providing a separation conduit having a separation matrix disposed therein;~~

~~transporting a first sample material through the separation conduit to separate the first sample material into a first plurality of different fractions;~~

~~replacing at least a portion of the separation matrix within the separation conduit~~ after separating the first sample material into a plurality of fractions; and

~~transporting a second sample material through the separation conduit~~ channel, through the injection channel, into the separation channel to separate the second sample material into a second plurality of different fractions.

19. (currently amended) The method of claim 18, wherein less than 90 % of the separation matrix is replaced in the replacing step.

20. (currently amended) The method of claim 18, wherein less than 75 % of the separation matrix is replaced in the replacing step.

21. (currently amended) The method of claim 18, wherein less than 50 % of the separation matrix is replaced in the replacing step.

22. (currently amended) The method of claim 18, wherein less than 20 % of the separation matrix is replaced in the replacing step.

23. (currently amended) The method of claim 18, wherein less than 10 % of the separation matrix is replaced in the replacing step.

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24. (currently amended) The method of claim 18, wherein less than 5 % of the separation matrix is replaced in the replacing step.

25. (currently amended) The method of claim 18, wherein less than 1 % of the separation matrix is replaced in the replacing step.

26. (currently amended) The method of claim 18, wherein the separation conduit has at least one microscale cross-sectional dimension.

27. (currently amended) The method of claim 26, wherein the separation conduit channel is disposed in a microfluidic device.

28. (currently amended) The method of claim 18, further comprising:
~~providing a sample loading channel fluidly coupled to the separation conduit at an intermediate point in the sample loading conduit, the sample loading conduit having a loading end and a waste end;~~

applying a first pressure difference across the sample loading conduit channel to move the second sample material into the loading end of the sample loading channel and toward the waste end of the sample loading channel; and

applying a second pressure difference across the separation conduit injection channel to move the portion of the separation matrix out of the separation conduit channel toward the waste end of the ~~sample loading~~ injection channel.

29. (currently amended) The method of claim 28, wherein a negative pressure is applied to the waste end of the sample loading conduit channel, the negative pressure simultaneously supplying the first and second pressure differences.

30. (currently amended) The method of claim 28, wherein the first and second pressure differences are substantially the same, and wherein the separation conduit channel is dimensioned such that only the portion of the separation matrix is removed from the separation conduit channel during the steps of applying the first and second pressure differences.

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31. (currently amended) The method of claim 28, wherein separation ~~conduit-channel~~ is in fluid communication with a source of separation matrix, and applying the second pressure difference transports an amount of separation matrix into the separation conduit from the source of separation matrix.

32-47. (cancelled)

48. (currently amended) ~~A~~ The method of separating sample materials ~~claim 1, further comprising:~~

~~providing a microfluidic device having a sample loading channel and a separation channel, the separation channel being fluidly connected to the sample loading channel, and wherein the separation channel comprises a separation matrix disposed therein;~~

~~bulk flowing a fluid sample material into the sample loading channel;~~

~~transporting a volume of the sample material from the sample loading channel into the separation channel;~~

~~electrophoretically separating a sample material into separate fractions within the separation channel;~~

~~replacing at least a portion of the separation matrix in the separation channel after electrophoretically separating the first sample material; and~~

~~repeating the bulk flowing, transporting, injecting and electrophoretically separating steps with an additional a second sample material.~~

49. (original) The method of claim 48, wherein substantially all of the separation matrix is replaced during the replacing step.

50. (original) The method of claim 48, wherein less than 90% of the separation matrix is replaced ~~in~~ the replacing step.

51. (original) The method of claim 48, wherein less than 50% of the separation matrix is replaced.

52. (currently amended) The method of claim 48, wherein the ~~bulk flowing, transporting, injecting, electrophoretically separating,~~ and replacing steps are repeated for each of at least two additional sample materials.

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53. (currently amended) The method of claim 48, wherein the replacing step is carried out during the ~~sample loading~~transporting step.

54. (currently amended) The method of claim 53, wherein the ~~sample loading~~injecting step draws at least a portion of the separation matrix out of the separation channel and into the ~~sample loading~~injection channel, and draws a volume of separation matrix into the separation channel from a separation matrix reservoir that is in fluid communication with the separation channel, thereby replacing the portion of the separation matrix.